

Sex differences after paediatric mild traumatic injury (mTBI) using diffusion MRI neurite orientation dispersion and density imaging (NODDI)

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Background: Following paediatric mTBI, girls may be at increased risk for longer recovery times and persistent symptoms (1, 2). We aim to explore the use of neurite orientation dispersion and density index (NODDI), an advanced diffusion MRI technique to uncover white matter (WM) microstructural differences between girls and boys after mTBI.

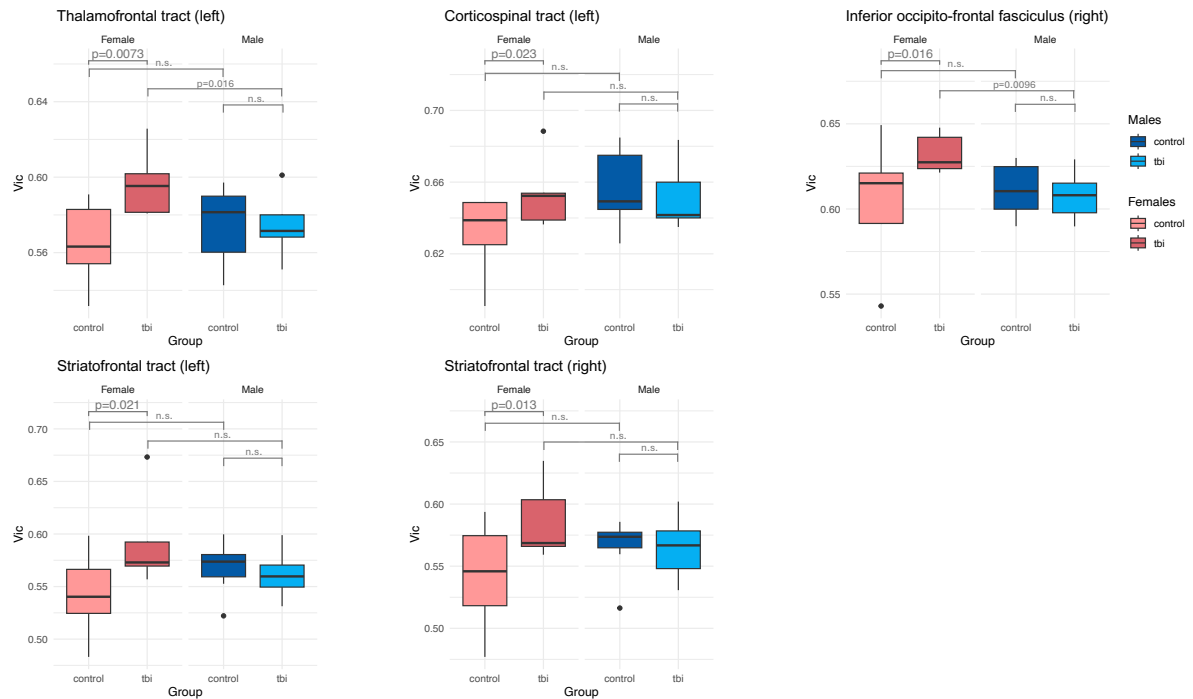
Materials & methods: 12 children acutely after mTBI (< 72h post-injury; 58% male, mean age = 13.4 ± 3.29 years) and 12 typically developing controls (58% male, mean age 13.5 ± 3.26 years) underwent imaging in a 3T MRI scanner (PRISMA, Siemens) using a multi-shell diffusion weighted imaging protocol (108 gradients, 5 b-value-shells, voxel-size 1.5mm³). Using a 2-tensor Unscented Kalman Filter Algorithm from the PNLNYPipe, NODDI metrics were obtained for 65 cerebral WM tracts. Exploratory multiple linear regression models for the 3 main NODDI metrics (volume of intracellular fraction (Vic), orientation dispersion index (ODI) and volume of isotropic diffusion (Viso)) investigated differences between girls (mean age = 12.4 ± 3.89) and boys (mean age = 14.2 ± 2.47) with mTBI, compared to controls while controlling for age, in-scanner motion and handedness. Post-hoc tests were run for the tracts with significant sex differences.

Results: 8 tracts, including the superior longitudinal fasciculus, and the corticospinal and frontostriatal tracts, had significant interactions between sex and study group in either Vic (5 tracts), ODI (3 tracts) or Viso (1 tract). Post-hoc tests showed that female mTBI patients had higher Vic and ODI values compared to male mTBI patients and controls of both sexes (p < .05) (Figure 1).

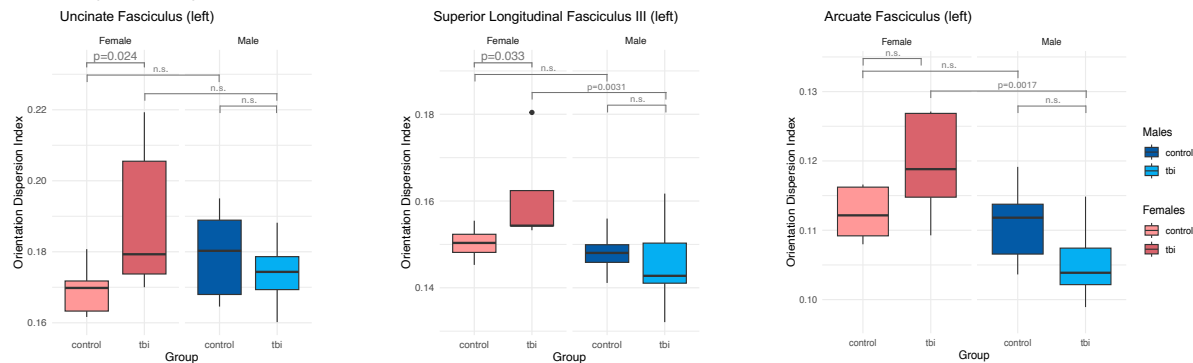
Conclusion: The exploratory results of this study highlight that NODDI may be more sensitive to sex-specific changes in WM microstructure after paediatric mTBI. Future studies should increase the sample size and consider pubertal development.

Figure 1: All tracts with significant interactions between sex and group for the three NODDI metrics (Vic, ODI & Viso).

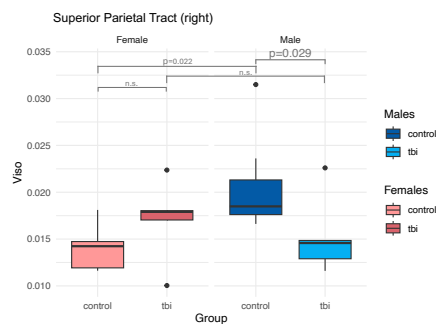
Tracts with significant study group and sex interactions



Tracts with significant study group and sex interactions



Tracts with significant study group and sex interactions



References:

1. Michael Kay JJ, Melton C, Holloway J, Moore D. Gender differences in outcome following pediatric concussion. *Neurology* [Internet]. 2018 Dec 4 [cited 2025 Aug 26];91(23_Supplement_1). Available from: <https://www.neurology.org/doi/10.1212/01.wnl.0000550680.93221.7c>
2. Clair R, Levin Allen S, Goodman A, McCloskey G. Gender differences in quality of life and symptom expression during recovery from concussion. *Applied Neuropsychology: Child*. 2020 Jul 2;9(3):206–14.